WNT4 gene

Wnt family member 4

Normal Function

The *WNT4* gene belongs to a family of WNT genes that play critical roles in development before birth. WNT genes provide instructions for making proteins that participate in chemical signaling pathways in the body. These pathways control the activity of certain genes and regulate the interactions between cells during embryonic development.

The *WNT4* gene provides instructions for producing a protein that is important for the formation of the female reproductive system, the kidneys, and several hormone-producing glands. During the development of the female reproductive system, the WNT4 protein regulates the formation of the Müllerian ducts, which are structures in the embryo that develop into the uterus, fallopian tubes, cervix, and the upper part of the vagina. This protein is also involved in development of the ovaries, from before birth through adulthood, and is important for development and maintenance of egg cells (oocytes) in the ovaries. In addition, the WNT4 protein regulates the production of male sex hormones (androgens).

Health Conditions Related to Genetic Changes

Dupuytren contracture

Müllerian aplasia and hyperandrogenism

At least three mutations in the *WNT4* gene have been found to cause Müllerian aplasia and hyperandrogenism, a condition that affects the reproductive system in females. Girls and women with this condition typically have an underdeveloped or absent uterus and do not menstruate. They may also have abnormally high levels of androgens, which can cause acne and excessive facial hair.

WNT4 gene mutations involved in Müllerian aplasia and hyperandrogenism change single protein building blocks (amino acids) in the WNT4 protein. Researchers suspect that the altered protein cannot be released from cells as it normally would be; the trapped protein is unable to perform its usual functions. Loss of regulation by WNT4 likely disrupts development of the female reproductive system and induces abnormal production of androgens, leading to the features of Müllerian aplasia and hyperandrogenism.

other disorders

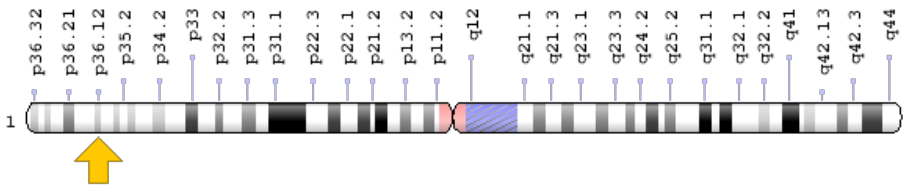
A mutation in the *WNT4* gene has been found to cause a severe condition called SERKAL (SEx Reversal and abnormal development of Kidneys, Adrenals, and Lungs) syndrome. In this condition, male sex development may occur despite the chromosome pattern typical of females. SERKAL syndrome has been reported in only one family and likely is not compatible with life. The mutation that causes SERKAL syndrome replaces the protein building block (amino acid) alanine with the amino acid valine at position 114 in the WNT4 protein (written as Ala114Val or A114V). This mutation is present in both copies of the *WNT4* gene in each cell and likely eliminates the function of the WNT4 protein. The absence of WNT4 protein results in the wide variety of developmental abnormalities seen in SERKAL syndrome.

A duplication of genetic material in a specific region of chromosome 1 can result in an extra copy of the *WNT4* gene. Having an additional copy of this gene leads to the production of extra WNT4 protein. People with this duplication may develop some female features despite having the chromosome pattern typical of males. These individuals can have an underdeveloped uterus and nonfunctional testes.

Chromosomal Location

Cytogenetic Location: 1p36.12, which is the short (p) arm of chromosome 1 at position 36.12

Molecular Location: base pairs 22,117,305 to 22,143,981 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- wingless-type MMTV integration site family member 4
- wingless-type MMTV integration site family, member 4
- WNT-4

- WNT-4 protein
- WNT4_HUMAN

Additional Information & Resources

Educational Resources

- Developmental Biology (sixth edition, 2000): Wnt4: a potential ovary-determining gene on an autosome
  https://www.ncbi.nlm.nih.gov/books/NBK9967/#A4122

GeneReviews

- Nonsyndromic Disorders of Testicular Development
  https://www.ncbi.nlm.nih.gov/books/NBK1547

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28WNT4%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- 46,XX SEX REVERSAL WITH DYSGENESIS OF KIDNEYS, ADRENALS, AND LUNGS
  http://omim.org/entry/611812
- WINGLESS-TYPE MMTV INTEGRATION SITE FAMILY, MEMBER 4
  http://omim.org/entry/603490

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_WNT4.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=WNT4%5Bgene%5D
- HGNC Gene Family: Endogenous ligands
  http://www.genenames.org/cgi-bin/genefamilies/set/542
- HGNC Gene Family: Wnt family
  http://www.genenames.org/cgi-bin/genefamilies/set/360
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12783

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/54361
- UniProt
  http://www.uniprot.org/uniprot/P56705

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Reviewed: July 2014
Published: March 21, 2017

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